



Herbal Immunomodulators: A Review

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ABSTRACT

Immunity is the protective response of our body to the antigen. The traditional Indian system of medicine (Ayurveda) describes different methods involved in the prevention and treatment of disease which are consequence of diet, life style and drugs as cornerstones of therapy. Herbal products are known to modify different aspects of human physiology and exert an alleviating influence on several patho-physiological states including modulation of immune system. In recent years, studies on evaluation of the therapeutic and toxic activity of herbal medicinal products became available and popular. Several herbs have proven immuno-modulating effects in severe conditions like HIV. Present review summarizes different data with respect to herbal immuno-modulators in various disease conditions.

Keywords: Immunomodulators, HIV, herbs, Neem, *Terminallia chebula*.

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INTRODUCTION

Immunity is a protective response of our body to any foreign substance which is identified as an antigen. Immunity is acquired or innate. It varies from person to person or amongst group of people belonging to different races. Immunity is provided by various superficial barriers like skin (uppermost layer) or by macrophages which show action of phagocytosis. Acquired immunity demonstrates a few features like specificity, diversity, memory and recognition. Immune system consists of a network of different lymphoid organs and cells. Primary lymphoid organs are bone marrow and thymus whereas secondary lymphoid organs consist of spleen and lymphnodes ¹.

Cells in immune system and their roles:

Different cells responsible in showing immune responses are:

T- cells:

CD4+ T- cells are responsible for co-ordination of immunological response of body to different antigens. Their main function is to secrete special factors which stimulate other white blood cells to fight a particular infection. CD8+ T- cells or more commonly known as killer T-cells are responsible for directly killing certain tumor cells.

Natural killer cells:

Natural killer cells unlike killer T-cells attack their target tumor cells without any prior conferencing in lymphoid organs. They directly kill tumor cells in lymphomas, mylenomas and also virus infected cells.

B cells:

The major functions of these cells is production of antibodies against different antigens like viruses, bacteria's etc

Granulocytes or Plymorphonuclear lymphocytes:

Granulocytes include three different types of cells namely basophils, nucleophils and eosinophils which are mostly responsible for removal of bacteria and parasites from the body.

Macrophages:

Macrophages referred as scavengers or antigen-presenting cells often act by engulfing the foreign material and presenting their antigen to T and B cells. They help in regulation of immune system ^{2,3}.

Immunomodulatory agents

Immunomodulation is the altering immune system in a positive or negative way by administration of drugs. Various immunomodulators are immunosuppressants, immunoadjuvants etc. Different uses of these agents are given as follows:

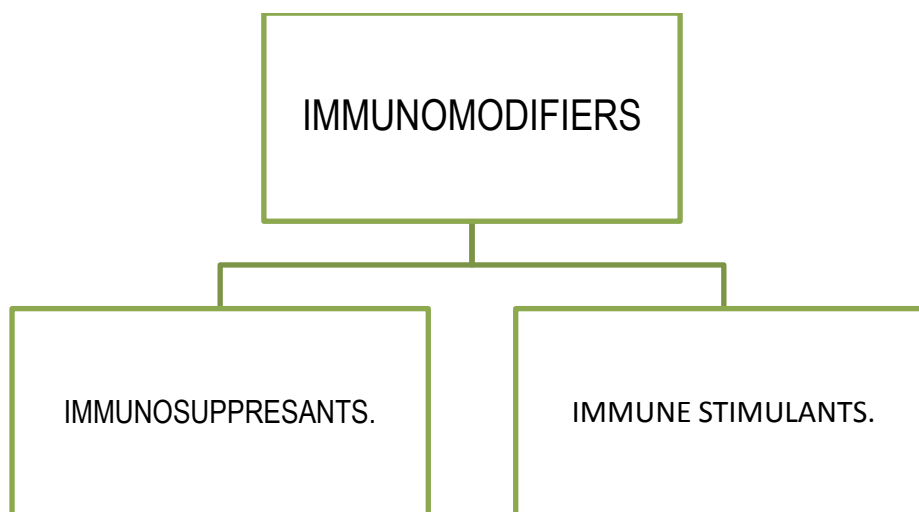
Immunomodulatory agents: These are agents or drugs which positively or negatively act on the immune system of our body by potentiating its response. These drugs maintain a balance in our immune system and a ready immune system does not give enough time for the invaders to build up an army and attack.

Immunostimulants:

These are agents which potentiate the immune responses of our body. They are non-specific in nature and can act through both innate and acquired immunity responses.

Immunosuppressants:

These are heterogeneous group of agents both structurally and functionally which affect immune system in a negative manner by suppressing its action. They are mainly used in different organ transplant surgeries and in regimens to treat certain diseases⁴.



Herbal immunomodulators: Introduction and mechanism of action.

Herbs are used since ancient time not only as food but also as medicines. Now-a-days research is more focused on herbs which act as immunomodulating agents. Various herbs as *Withania somnifera*, *Panax ginseng*, *curcuma longa* and many others are studied for their immunomodulatory effect. Effects of these various herbs on different components of immune system are given as follows:

Effect on T cells:

T cells have been considered most important as their activation requires antigen specificity and full activation requires signals from T cell receptor and other co-stimulatory factors. Various Chinese herbs act as immunosuppressants and are used in therapy for cancer ⁵.

Effect on Cytokine production:

A network of cytokine is important in regulation of immune responses. Different types of cytokines are mainly produced by T cells. Based on synthesis of various cytokines T cells are classified as: Th1 cells producing IL-2 and IFN- γ and Th2 cells producing IL-4, IL-5 and IL-10. Both Th1 and Th2 T cells are susceptible to herbal immunomodulation ⁶.

Effect on antibody production:

Antibodies react with antigen and elucidate an immune response. Sometimes it is possible that may identify components of our body as antigens as seen in case of rheumatoid arthritis. Hence it is essential to know both immunosuppressant and immunostimulant herbs to tackle with this situation. Fun-boi (*Stephenia tetrandra*) and aqueous extract of *Trigonella foenum* are immunosuppressant and immuno-stimulant in action respectively ⁷.

Different herbal immunomodulators used in specific diseases

Herbal medicines have been used traditionally for curing different ailments. Rasayanas which are formulations of immunomodulatory drugs mentioned in Ayurveda have attracted attention of scientists in recent times. Different immunomodulatory drugs and their specific action are mentioned in the following table:

Table 1: Various herbal immuno-modulators ^{8,9}

Name of drug	Botanical name	Active chemical constituent	Uses
Neem	<i>Azadirachta indica</i> . Family: Meliaceae.	_____	Used against cytotoxic drugs as immunostimulant.
Ashwagandha	<i>Withania somnifera</i> . Family: Solanaceae.	Withanolides	Immunostimulants to counteract undesirable effects of myelosuppressive drugs.
Ginseng	<i>Panax ginseng</i> . Family: areliaceae.	Ginsenosides.	Immunostimulatory.
Guduchi	<i>Tinospora cordifolia</i> . Family: menispermaceae.	Cordifolioside A	Used in rheumatoid arthritis.
Shatavari.	<i>Asparagus racemosus</i> . Family: liliaceae.	Shatavarin IV	Immunostimulant and used in arthritis.
Amla	<i>Emblica officinalis</i> . Family: Euphorbiaceae.	Ascorbic acid	Immunomodulator.

Screening of herbal immunomodulators

Screening of immunomodulators involves a routine process of extraction of active constituents from the source and then screening it by different in-vitro and in-vivo methods which also includes checking the drug in an animal model. Different in-vivo and in-vitro methods of biological screening are:

***In vitro* methods**

1. Test for inhibition of histamine release from mast cells
2. Mitogens induced lymphocyte proliferation test.
3. Test for checking inhibition of T cell proliferation
4. PFC (plaque forming colony) test *in vitro*
5. Inhibition of dihydro-orotate dehydrogenase test.

***In vivo* methods**

1. Test for checking spontaneous autoimmune diseases in animals
2. Study of acute systemic anaphylaxis in rats
3. Anti-anaphylactic activity (Schultz-Dale reaction) for checking immuno-modulatory effect of plant.
4. Reversed passive arthus reaction
5. Study of Arthus type immediate hypersensitivity
6. Delayed type hypersensitivity test.
7. Passive cutaneous anaphylaxis test.
8. Collagen type II induced arthritis in rats.
9. Proteoglycan-induced progressive polyarthritis in mice
10. Coxsackievirus B3-induced myocarditis myocarditis in rats
11. Porcine cardiac myosin-induced autoimmune test.
12. Experimental allergic encephalomyelitis test.
13. Study of acute graft versus host disease (GVHD) in rats.
14. Study of influence on SLE-like disorder in MRL/lpr mice
15. Prevention of experimentally induced myasthenia gravis in rats
16. Glomerulonephritis induced by antibasement membrane antibody in rats
17. Auto-immune uveitis in rats
18. Inhibition of allogenic transplant rejection ¹⁰.

Herbal immunomodulators in HIV

Human Immunodeficiency Virus/Aquired Immunodeficiency Syndrome (HIV/AIDS) is still one of the major public health problems particularly in the sub-Saharan Africa. HIV virus attacks and

impairs the body's natural defense system against disease and infection. The underlying problem identified as a severe depression of immune system that is cause by the nearly complete lack of one class of T-lymphocyte, which are called helper cell that are needed for initiating and maintaining many immune responses. Every day over 6800 persons become infected with HIV and over 5700 persons dying from AIDS. Herbs used in therapy of AIDS are:

Table: 2 Herbal immunomodulators used in AIDS ¹¹.

Sr.no:	Name of plant	Part of plant used:	Active constituents	Activity
1.	<i>Andrographis paniculata</i>	Aerial part	Andrographolide, bicyclic diterpenoid, lactone and kalmeghin	Immunostimulant Inhibited syncytium formation, Anti HIV activity.
2.	<i>Momardica charantia</i>	Seeds	MAP 30 (Momardica Anti HIV protein), Alpha momarcharin, MRK 29 (RIP), momardicosides	RT activity, inhibits HIV-1 infection, syncytium formation, herpes simplex virus, HIV-1 integrase, Beta glucosidase inhibitory.
3.	<i>Phyllanthus niruri</i>	Whole plant	Phyllanthin, Hypophyllanthin, Rapendusinic acid A monosodium salt (RA)	HIV-1 inhibitor, Inhibite HIV-1 RT
4.	<i>Terminallia chebula</i>	Fruit	Gallic acid, Ellagic acid, Chebulic acid, Galloyl glucoses	HIV-1 Integrase, Inhibitor of HIV-1 Protease
5.	<i>Glycyrrhiza glabra</i>	Roots	Glycyrrhizin	Anti HIV activity, Inhibits HIV induce plaque Formation

CONCLUSION

Immune system is a complex system which is required for protection of our body from various different antigens. Immune system comprises of different cells and organs involved in immune responses. A proper balance between immunosuppression and immunostimulation is required to be maintained. Immunomodulation is required during conditions like organ transplant, AIDS, tuberculosis etc. Allopathic drugs have an appreciable immunomodulatory effect but show harmful toxic effects also. Various herbs are being explored for their immunomodulatory activities. Herbs provide good immunomodulatory effect without any toxic effects or drug interactions. Effective herbs have been discovered and used now-a-days for immunomodulation in different conditions. Use herbal immunomodulators will be more beneficial for the masses.

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